

**AMENDMENTS TO THE CLAIMS**

1. **(Original)** A method for detecting a risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual by determining a variant polymorphic form in a GPRA gene, comprising the steps of
  - a) providing a biological sample taken from the individual to be tested,
  - b) detecting the presence or absence of a variant polymorphic form in a GPRA gene in the biological sample, the presence of the variant genotype indicating an increased risk of said disease in said individual.
2. **(Original)** The method of claim 1, wherein the variant form occurs in a noncoding region of the GPRA gene
3. **(Original)** The method of claim 1, wherein the variant form occurs in a coding region of the GPRA gene
4. **(Original)** The method of claim 1, wherein the variant form occurs between introns 3 and 4 of the GPRA gene.
5. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a variant form relative to any of SEQ ID NOS: 1, 3, 5, 7, 9, 11 and 13.
6. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a variant form relative to any of SEQ ID NOS: 5, 7, 11 and 13.
7. **(Original)** The method of claim 1, wherein the method comprises determining whether said sample contains a haplotype selected from the group consisting of: H2, 114, and 115.
8. **(Original)** The method of claim 1, wherein the variant form is a variant form shown in Table 3.

9. **(Original)** The method of claim 8, wherein the variant form is at a polymorphic site shown in Table 3.

10. **(Original)** The method of claim 1, wherein the variant form is a variant form shown in Table 7.

11. **(Original)** The method of claim 1, wherein the variant form is a variant form at a polymorphic site not designated \* in Table 7.

12. **(Original)** The method of claim 1, wherein the method comprises a step of determining whether said sample contains polymorphic forms relative to SEQ ID NO:1 at each of a plurality of polymorphic sites within the AST-1 locus, the presence of variant polymorphic forms at two or more of the plurality of polymorphic sites indicating increased risk of said disease.

13. **(Original)** The method of claim 1, further comprising determining whether said sample contains a variant polymorphic form in an AAA1 gene, wherein the presence of the variant polymorphic form in the AAA1 gene indicates risk of said disease.

14. **(Original)** The method of claim 13, wherein the variant polymorphic form occurs in the coding region of the AAA1 gene.

15. **(Original)** The method of claim 1, further comprising amplifying at least part of SEQ ID NO: 1 (AST-1) locus including the polymorphic site before the determining step.

16. **(Original)** The method of claim 1, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

17. **(Original)** The method of claim 1, wherein said disease is COPD or asthma.
18. **(Withdrawn, Original)** A method for identifying a polymorphic site correlated with a disease selected from the group consisting of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease or susceptibility thereto, comprising: identifying in vitro a polymorphic site within a GPRA or AAA1 gene, determining whether a variant polymorphic form occupying the site is associated with the disease or susceptibility thereto.
19. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs in a noncoding region of the GPRA or AAA1 gene
20. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs in a coding region of the GPRA or AAA1 gene
21. **(Withdrawn, Original)** The method of claim 18, wherein the variant form occurs between introns 2 and 4 of the GPRA gene.
22. **(Withdrawn, Original)** The method of claim 18, wherein the determining is performed by comparing the frequency of the variant polymorphic form in samples taken from individuals with and without the disease.
23. **(Withdrawn, Original)** The method of claim 18, wherein said disease is COPD or asthma.
24. **(Currently Amended)** Use of a A kit for diagnosing or assessing predisposition to a pulmonary disease associated with lower airways obstruction or an IgE mediated disease, said kit comprising;

a container; and in the container:

a compound, preferably labeled, capable of detecting a polymorphic form at a polymorphic site in a susceptibility locus for asthma as defined by SEQ ID NO:2 or 4.

25. **(Currently Amended)** The use-kit of claim 24, wherein the polymorphic site occurs at a position shown in Table 3, Table 7, Table 12, Table 13 or Table 14.

26. **(Currently Amended)** The use-kit of claim 24, wherein said compound is capable of detecting a polymorphic form at a polymorphic site in a GPRA gene.

27. **(Currently Amended)** The use-kit of claim 26, wherein the polyformic form comprises the sequence set forth in any of SEQ ID NOS: 1, 3, 5, 7, 9, 11 and 13.

28. **(Currently Amended)** The use-kit of claim 27, wherein the polyformic form comprises the sequence set forth in SEQ ID NOS: 5, 7, 11 and 13.

29. **(Currently Amended)** The use-kit of claim 26, wherein the polyformic form comprises a haplotype selected from the group consisting of: H2, H4, and H5.

30. **(Withdrawn, Original)** The use of claim 24, wherein said compound is capable of detecting a polymorphic form at a polymorphic site in an AAA1 gene.

31. **(Withdrawn, Original)** The use of claim 30, wherein the polyformic form comprises the sequence set forth in SEQ ID NOS: 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 and 40.

32. **(Currently Amended)** The use-kit according to claim 24, wherein the compound is a primer or probe.

33. **(Currently Amended)** The use-kit according to claim 24, wherein said disease is COPD or asthma.

34. **(Withdrawn, Original)** A method for detecting a risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual by determining a variant polymorphic form in an AAA1 gene, comprising the steps of  
a) providing a biological sample taken from the individual to be tested,  
detecting the presence or absence of a variant polymorphic form in an AAA1 gene in the biological sample, the presence of the variant genotype indicating an increased risk of said disease in said individual.

35. **(Withdrawn, Original)** The method of claim 34, wherein the determining comprises determining whether the individual has a variant form relative to any of SEQ ID NOS: 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38 and 40.

36. **(Withdrawn, Original)** The method of claim 34, wherein the determining comprises determining whether the individual carries a haplotype selected from the group consisting of: H2, H4, and H5.

37. **(Withdrawn, Original)** The method of claim 34, wherein the variant form is a variant form shown in Table 12.

38. **(Withdrawn, Original)** The method of claim 34, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

39. **(Withdrawn, Original)** The method of claim 34, wherein said pulmonary disease is COPD, asthma, or other IgE mediated disease.

40. **(Withdrawn, Original)** A method for identifying of any one of haplotype combinations H1 to H7 as defined in Tables 13 and 14 comprising the steps of:

- a) providing a biological sample;
- b) detecting the presence of AST1 markers in the biological sample, said markers being selected from the SNPs listed in Tables 13 and 14.

41. **(Withdrawn, Original)** The method of claim 40, wherein said SNPs are located in the following positions in contig NT 000380: 515224 (position 5442 in SEQ ID NO:1), 522363 (position 12581 in SEQ ID NO:1), 529556 (position 19774 in SEQ ID NO:1), 546333 (position 36551 in SEQ ID NO:1), 555608 (position 45826 in SEQ ID NO:1), 563704 (position 53922 in SEQ ID NO:1), and 585883 (position 76101 in SEQ ID NO:1).

42. **(New)** A method for determining risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease in an individual, comprising;

determining whether a biological sample from an individual contains haplotypes H2, H4, H5, and H7 in the AST-1 locus as defined by SEQ ID NO:1, the presence of at least one of said haplotypes in the sample indicating risk of a pulmonary disease associated with lower airways obstruction or an IgE mediated disease, wherein

i) haplotype H2 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);

- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide G located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

ii) haplotype H4 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide A located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide C located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

iii) haplotype H5 is defined by the following polymorphisms:

- nucleotide C located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);

- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and
- nucleotide C located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1);

iv) haplotype H7 is defined by the following polymorphisms:

- nucleotide G located in position 515224 in contig NT\_000380 (i.e. position 5442 in SEQ ID NO:1);
- nucleotide C located in position 522363 in contig NT\_000380 (i.e. position 12581 in SEQ ID NO:1);
- nucleotide A located in position 529556 in contig NT\_000380 (i.e. position 19774 in SEQ ID NO:1);
- nucleotide G located in position 546333 in contig NT\_000380 (i.e. position 36551 in SEQ ID NO:1);
- nucleotide T located in position 555608 in contig NT\_000380 (i.e. position 45826 in SEQ ID NO:1);
- nucleotide C located in position 563704 in contig NT\_000380 (i.e. position 53922 in SEQ ID NO:1); and

- nucleotide G located in position 585883 in contig NT\_000380 (i.e. position 76101 in SEQ ID NO:1).

43. (New) The method of claim 42, wherein the presence of at least one of said haplotypes is determined by identifying a polymorphic site occurring in a position listed in Table 14.

44. (New) The method of claim 42, wherein the determining is performed by allele specific amplification, allele specific hybridization, single strand conformation polymorphism (SSCP), oligonucleotide ligation assay, single-base extension assay, or restriction fragment length polymorphism (RFLP).

45. (New) The method of claim 42, wherein said disease is chronic obstructive pulmonary disease (COPD) or asthma.